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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/053,230	01/16/2002	Xianqiang Li	26757-706	3906

21971 7590 12/21/2004

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EXAMINER	
SISSON, BRADLEY L	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 12/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/053,230	LI ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-42 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Attention is directed to the decision in *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428:

> To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Vas-Cath, 935 F.3d at 1563; see also Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); In re Gosteli, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572.

3. For convenience, claims 1, 17, 18, 32, and 35, the only independent claims, are reproduced below.

1. (Currently Amended) A method for selecting cells based on whether the cells express a short-lived protein, the method comprising:

i) expressing a different fusion protein in each cell within a library of cells, the fusion protein comprising a reporter protein and a protein encoded by a sequence from a cDNA library derived from a sample of cells, and the sequence from the cDNA library varying within the cell library;

ii) inhibiting further expression of the fusion protein to allow the expressed fusion protein to degrade in the cell; and

iii) selecting a population of cells from the library of cells based on the population of cells having different reporter signal intensities than other cells in the library, the difference being indicative of the population of cells expressing shorter lived fusion proteins than the fusion proteins expressed by the other cells in the library.

17. (Currently Amended) A method for selecting cells based on whether the cells express a short-lived protein, the method comprising:

expressing a first reporter protein and a different fusion protein in each cell within a library of cells, the fusion protein comprising a second reporter protein and a protein encoded by a sequence from a cDNA library derived from a sample of cells, and the sequence from the cDNA library varying within the cell library;

inhibiting further expression of the first reporter protein and the fusion protein to allow the expressed fusion protein to degrade in the cell; and

selecting a population of cells from the library of cells based on the population of cells having different normalized reporter signal intensities than other cells in the library, the normalized reporter signal intensity comprising a reporter signal from the fusion protein normalized relative to a reporter signal from the first reporter protein, the difference being indicative of the population of cells expressing shorter lived fusion proteins than the fusion proteins expressed by the other cells in the library.

18. (Currently Amended) A method for selecting cells based on whether the cells express a short-lived protein, the method comprising:

taking a library of cells, the cells in the library expressing a different fusion protein comprising a reporter protein and a protein encoded by a sequence from a cDNA library derived from a sample of cells, the sequence from the cDNA library varying within the cell library;

partitioning the library of cells into populations of cells based on an intensity of a reporter signal from the fusion protein such that cells partitioned into a given population have a reporter signal within a range of reporter signal intensity;

inhibiting further expression of the fusion protein to allow the expressed fusion protein to degrade in the given population of cells; and

selecting a subpopulation of cells from the given population of cells based on the subpopulation of cells having different reporter signal intensities than other cells in the given population, the difference being indicative of the subpopulation of cells expressing shorter lived fusion proteins than the fusion proteins expressed by the other cells in the given population.

32. (Currently Amended) A method for selecting cells based on whether the cells express a short-lived protein, the method comprising:

taking a library of cells, the cells in the library expressing a first reporter protein and a different fusion protein comprising a second reporter protein and a protein encoded by a sequence from a cDNA library derived from a sample of cells, the sequence from the cDNA library varying within the cell library;

partitioning the library of cells into populations of cells based on an intensity of a reporter signal from the fusion protein such that cells partitioned into a given population have a reporter signal within a desired range of reporter signal intensity;

inhibiting further expression of the fusion protein to allow the expressed fusion protein to degrade in the given population of cells; and

selecting a subpopulation of the cells from the given population of cells based on whether the cells have different normalized reporter signal intensities than other cells in the given population, the normalized reporter signal intensity comprising a reporter signal from the fusion protein normalized relative to a reporter signal from the first reporter protein, the difference being indicative of the subpopulation of cells expressing shorter lived fusion proteins than the fusion proteins expressed by the other cells in the given population.

35. (Currently Amended) A method for selecting cells based on whether the cells express a short-lived protein, the method comprising:

forming a construct library encoding a library of different fusion proteins, each fusion protein comprising a reporter protein and a protein encoded by a sequence from a cDNA library derived from a sample of cells;

transducing or transfecting the construct library into cells to form a library of cells which express the library of the fusion proteins;

screening the transduced or transfected cells for cells which express the fusion protein;

partitioning the screened cells into populations of cells based on an intensity of a reporter signal from the fusion protein such that cells partitioned into a given population have a reporter signal within a desired range of reporter signal intensity;

inhibiting further expression of the fusion protein to allow the expressed fusion protein to degrade in the given population of cells; and

selecting a subpopulation of the cells from the given population of cells based on whether the cells have different reporter signal intensities than other cells in the given population, the difference being indicative of the subpopulation of cells expressing shorter lived fusion proteins than the fusion proteins expressed by the other cells in the given population.

4. For purposes of examination, the claims have been interpreted as encompassing the selection of any cell from any life form, be it single or multicellular, and wherein the multicellular life form fairly encompasses all life forms, including but not limited to all insects, invertebrates, lichens, amphibians, birds, fishes, and mammals, and wherein said mammals fairly encompasses duckbill platypi, whales, dolphins, monkeys, primates and humans. Said method claims have also been interpreted as encompassing the simultaneous monitoring and selection of each and every "short-lived protein" in said cells and where aid cells are optionally combined into a common library of cells. Said method claims have also been interpreted as encompassing the requisite analyzing where but a single reporter protein is used and that the reporter protein is

not necessarily expressed or in genetic linkage to a short-lived protein(s) encoded by the cell's genome.

5. A review of the disclosure finds reference has been made to several non-patent documents; see pages 22, 30, and 31. None of thee documents have been incorporated by reference and therefore cannot be relied upon for satisfaction of the written description or enablement requirements of 35 USC 112, first paragraph.

6. While there is no *per* se rule that an applicant must provide an example of each and every permutation encompassed by their claims, the disclosure still must provide an adequate written description of the requisite starting materials and directions as to how they are to be used such that the full scope of the invention is described in such full, clear, concise, and exact terms and reasonably so as to reasonably suggest that the claimed invention was in applicant's possession at the time of filing. While the specification does provide drawings, and makes reference t them in the prophetic examples, the figures lack the full, clear, concise and exact terminology so as to clearly identify the starting materials and methods of operation that permit the full scope of the invention to be practiced. It appears that applicant is attempting to satisfy the written description requirement of 35 USC 112, first paragraph, through obviousness. Obviousness, however, cannot be relied upon for satisfaction of the written description requirement. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966:

> Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

7. For the above reasons, and in the absence of convincing evidence to the contrary, claims 1-42 are rejected under 35 USC 112, first paragraph, as failing to comply with the written description requirement.

Response to argument

8. At page 12, bridging to page 13 of the response received 22 September 2004, hereinafter he response, applicant's representative asserts that a "general scheme of the screening assay" is provided via pages 12-14 and Figure 1 of the instant application.

9. The above response has been fully considered and has not been found persuasive towards the withdrawal of the rejection. While the disclosure may provide a "general scheme," such general teachings have not been found to provide the requisite full, clear, and concise description required in order to reasonably suggest that applicant was in possession of the full scope of the presently claimed invention.

10. A review of the disclosure, and a review of applicant's representative's remarks fail to identify where the disclosure teaches the broad genus of starting materials that result in a useful product. While applicant/declarant has provided a showing of how the claimed assay can be conducted, the disclosure of the instant application fails to teach in suffi9cent terms how one is to recognize a useful product from that which is not useful, and/or unknown, and is the subject of further investigation.

11. For the above reasons, and in the absence of convincing evidence to the contrary, claims 1-42 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

12. Claims 1-42 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As set forth in *Enzo Biochem Inc., v. Calgene, Inc.* (CAFC, 1999) 52 USPQ2d at 1135, bridging to 1136:

> To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, see *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).... We have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be "undue." See, *e.g.*, *Wands*, 858 F.2d at 736-37, 8 USPQ2d at 1404 ("Enablement is not precluded by the necessity for some experimentation . . . However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' ") (footnotes, citations, and internal quotation marks omitted). In *In re Wands*, we set forth a number of factors which a court may consider in determining whether a disclosure would require undue experimentation. These factors were set forth as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* at 737, 8 USPQ2d at 1404. We have also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling. See *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the *Wands* factors "are illustrative, not mandatory. What is relevant depends on the facts.").

13. As noted above, the disclosure has not been found to reasonably suggest that applicant was in possession of the invention at the time of filing. It is well settled that one cannot enable the practice of an invention that they do not yet possess, and that obviousness cannot be relied upon so to demonstrate that they possessed the invention.

It is further noted that in order to be enabling, the specification must set forth starting materials and reaction conditions. These critical elements are not to be found in the present disclosure and the cited prior art cannot be relied upon to overcome these deficiencies. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

> " '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').
>
> *****
>
> "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.
> "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. <u>However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art.</u> It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research. (Emphasis added)

14. Claims 1-42 are not enabled by the disclosure and to do so, which would require the identification and development of starting materials and reaction conditions would cause the skilled artisan to resort to trial-and-error experimentation. Such level of effort constitutes undue experimentation. Therefore, and in the absence of convincing evidence to the contrary, claims 1-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

15. Claims 1-42 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility

16. It is noted with particularity that while the claims are drawn to a method if "isolating and characterizing short-lived proteins," the end-product is not known and even when isolated and characterized, it remains to be seen just what function it serves. In short, the claimed method produces a product for which no utility has been shown to exist.

17. Claims 1-42 also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Response to argument

18. At page 13, bridging to page 14 of the response applicant's representative asserts that the instant disclosure provides an ample teaching of how to conduct the assay; attention is directed to pages 16-22 as well as to the Rule 1.131 declaration.

19. The above argument has been fully considered and has not been found persuasive for neither the specification, applicant's representative's remarks, nor the declaration teach how the method is to be practiced and useful results are obtained, and that one is able to recognize results that are useful when non-useful signals are also present.

20. The declaration filed on 22 September 2004 under 37 CFR 1.131 has been considered but is ineffective to overcome the rejection of claims under 35 USC 112, first paragraph, and under 35 USC 101.

21. The Declaration is that of a single individual, co-inventor Xianqiang Li, however, the declaration has been found to contain statements and showings that are attributable, at least in part, to the actions of another. Such statements and showings constitute hearsay and are not dispositive of the issues at hand.

22. Assuming *arguendo*, that the declaration was filed over the signatures of all relevant individuals, the declaration does not show how, based only upon the instant disclosure, one of skill in the art at the time of the invention would be able to identify useful fusion proteins that have a short life from those that are unknown and/or are the subject of further investigation, i.e., do not yet have any known utility.

23. For the above reasons, and in the absence of convincing evidence to the contrary, claims 1-42 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

Conclusion

24. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

25. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

27. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

28. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
19 December 2004